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POTASSIUM MOVEMENTS ASSOCIATED WITH AMINO ACID AND SUGAR TRANSPORT IN ENTEROCYTES ISOLATED FROM RABBIT JEJUNUM

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SUMMARY

1. Active transport of amino acids and the sugar, α-methyl-D-glucoside (α-MG) caused an increase in the rate of K efflux from isolated rabbit enterocytes. These effects were inhibited by apamin (5×10^{-7} M), quinidine (10^{-3} M), Ba (5×10^{-3} M) and trifluoperazine (5×10^{-5} M) but not by the loop diuretic furosemide (10^{-4} M). None of these drugs affected the basal rate of K efflux.

2. The stimulatory effects of amino acids or α-MG on K efflux are too great to be explained in terms of an increase in the electrical driving force across the plasma membrane of these cells and a change in membrane permeability is envisaged.

3. An apparent Ca-dependent K permeability in isolated enterocytes can be demonstrated using the Ca ionophore A23187. The effect of the ionophore on K efflux is abolished by apamin or Ba. It is proposed that Ca-dependent K channels mediate the sugar and amino acid induced increases of K efflux.

4. Under control conditions there is a decrease in intracellular K concentration during accumulation of alanine or α-MG. Ba by itself does not alter K concentration but it did produce a marked increase when used in conjunction with alanine or α-MG.

5. The accumulation of α-MG was inhibited in the presence of Ba. This is consistent with an interference with the driving force for sugar accumulation.

6. It is suggested that the increase in K permeability described has a role in both maintaining ion homoeostasis during Na-coupled transport and contributing to the driving force for sugar and amino acid absorption.

INTRODUCTION

An appealing feature of Koefed-Johnsen & Ussing's (1958) model for transepithelial ion transport was its initial simplicity. The model in which the Na–K pump and a series of leak pathways are responsible for the ion transport and for cellular homoeostasis has, however, at least one major drawback in that constant leak pathways leave the epithelial cells vulnerable to the accumulation of high osmotic loads during periods of transport activity. It has been proposed that the rates of Na ion entry at the apical membrane and K ion exit at the basolateral membrane of epithelia are controlled, and possibly linked. This would explain how the cell maintains its intracellular ion composition while engaged in the transepithelial transport (Taylor & Windhager, 1979; Schultz, 1981; Diamond, 1982).

Much evidence exists showing that intracellular Ca regulates Na entry at the apical membrane in some epithelia (Windhager & Taylor, 1983). Electrophysiological analysis has also produced indirect evidence suggesting that the K permeability of the basolateral membrane increases at periods of increased pump-mediated K entry into epithelial cells; e.g. during Cl secretion by canine tracheal epithelium (Smith & Frizzel, 1984) and during Na-coupled alanine transport by *Necturus* small intestine (Grasset, Gunter-Smith & Schultz, 1983). In addition to maintaining ion concentrations, an increase in basolateral membrane conductance may be partly or wholly responsible for the repolarization seen to occur after sugars and amino acids initially depolarize the apical membrane potential (Albus, 1980; Gunter-Smith, Grasset & Schultz, 1982).

Results suggestive of an increase in K permeability during Na-coupled transport were perhaps first reported by Brown & Parsons (1962) who showed that the actively transported sugars 3-*O*-methylglucose and galactose caused the K content of rat jejunal mucosa to fall. These results have since been reproduced using ion-sensitive micro-electrodes (Lee & Armstrong, 1972).

The present work uses a viable preparation of isolated rabbit jejunal enterocytes (Brown & Sepúlveda, 1985) to show that actively transported sugars and amino acids increase the K permeability of the cells. Evidence that Ca-dependent K channels may play a role in this phenomenon is also provided. Preliminary reports of part of this work have already appeared (Brown, Burton & Sepúlveda, 1983*a*, *b*; Brown & Sepúlveda, 1984).

METHODS

Cell isolation, uptake and efflux experiments

All experimental details are the same as those described in the preceding paper (Brown & Sepúlveda, 1985). It should be noted that in efflux experiments the cells were loaded in the presence of 5 μCi ^{86}Rb/ml and that enough mannitol was added to the control buffers to make them isotonic with the medium in test incubations. This manoeuvre did not appear to affect the rate of potassium efflux.

Materials

Analar grade chemicals were used throughout, quinidine hydrochloride, apamin, phloridzin, Ca ionophore A23187 and verapamil hydrochloride were all obtained from Sigma Chemical Co. (St. Louis U.S.A.). Trifluoperazine dihydrochloride was a generous gift from Smith, Kline and French Laboratories Ltd. (Welwyn Garden City, Herts.). Methyl(α-D-[U-^{14}C]gluco)pyranoside, 3-*O*-methyl-D-[U-^{14}C]glucose, ^{86}rubidium chloride, ^{42}potassium chloride and [^{3}H]inulin were purchased from Amersham International PLC, Amersham, Bucks.

RESULTS

Amino acids and sugars induce an increase in enterocyte membrane K permeability

Efflux of both ^{42}K and ^{86}Rb from pre-loaded suspensions of isolated rabbit enterocytes has been shown to follow the same single exponential function (Brown & Sepúlveda, 1985). Fig. 1 shows the effect of 20 mM-L-alanine upon the rate of efflux of both ^{42}K and ^{86}Rb from rabbit intestinal cells. The presence of L-alanine in the bathing solution caused a marked increase in the efflux of both isotopes. It is clear from Fig. 1 that ^{86}Rb mimicked the effect of alanine on ^{42}K efflux, suggesting that it is a suitable tracer for K. ^{86}Rb was used in all subsequent efflux experiments.

Rate constants for efflux under control conditions, measured in a number of different cell batches, ranged from 0·013 to 0·059/min (0·035±0·002/min, mean±S.D., $n = 29$), but remained constant in parallel measurements in the same batch of cells. L-alanine (20 mM) induced increases in the rate constant to up to 340% of the basal value. The mean increase for the rate constant in the presence of L-alanine was from 0·033±0·003 to 0·076±0·005/min (mean±S.E. of seventeen experiments)

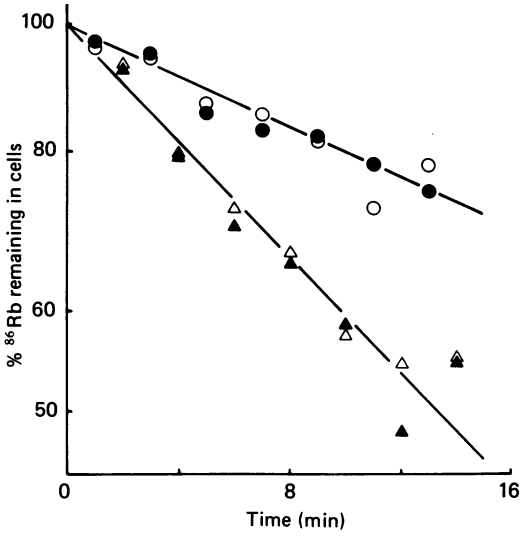

Fig. 1. Effect of alanine on ^{42}K and ^{86}Rb loss from rabbit enterocytes. Rabbit enterocytes were pre-loaded with ^{86}Rb and ^{42}K over a 25 min incubation and the isotope remaining associated with the cells was measured at timed intervals. Results are means of four experiments. The percentage of the initial ^{86}Rb (open symbols) or ^{42}K (filled symbols) content remaining is plotted on a logarithmic scale against time, in the presence (triangles) or absence (circles) of 20 mM-alanine.

which is equivalent to 230% of the mean control value. This difference was statistically significant ($P < 0·001$, paired t test). Table 1 shows the effect of six other amino acids on K efflux. Clearly the ability to induce increases of the rate constant of K efflux is not an exclusive property of L-alanine. It is also interesting to note that the amino acids causing the greatest increase are those whose transport has a high Na dependency (Sepúlveda & Smith, 1978); L-lysine and L-arginine showing low Na dependence had little effect. The non-metabolizable sugar, α-methyl-D-glucoside (α-MG), used at a concentration of 5 mM, also induced an increase in the rate of efflux from 0·036±0·006 to 0·082±0·014/min (mean±S.E., $n = 6$), an average increase of 230% of the basal value ($P < 0·01$ by paired t test). As has previously been shown phloridzin, a specific inhibitor of Na-dependent hexose transport, abolishes the α-MG-induced stimulation of ^{86}Rb release (Brown *et al.* 1983*b*). This suggests that the increase is related to Na-dependent transport of the sugar and not merely to its presence in the extracellular fluid. The effects of α-MG and L-alanine are not additive when both are present in the bathing medium (results not shown).

Inhibition of the effects of sugars and amino acids on K efflux

Apamin, a peptide neurotoxin isolated from bee venom, has been shown to block Ca-dependent K channels in a number of cells including the guinea-pig hepatocyte (Burgess, Claret & Jenkinson, 1981), a mouse neuroblastoma cell (Hugues, Romey, Duval, Vincent & Lazdunski 1982*a*) and rat brain synaptosomes (Huges, Duval,

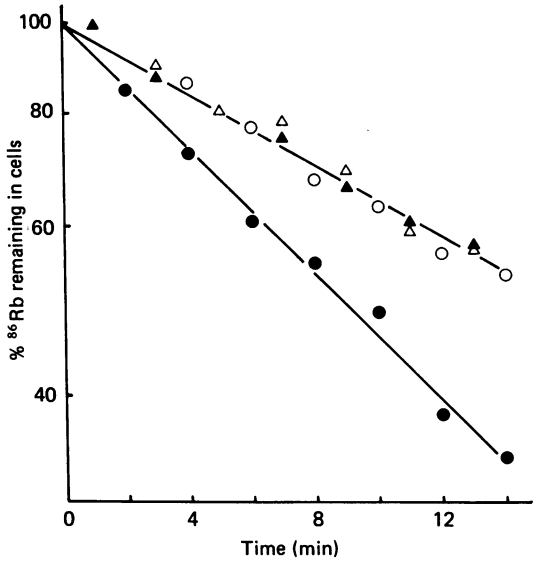

Fig. 2. Effect of apamin on the alanine-dependent increase in K efflux by rabbit enterocytes. The experiment was performed as that in Fig. 1, but in the presence of 20 mM-D-mannitol (▲,△) or 20 mM-alanine (●,○) in the presence (open symbols) or absence (filled symbols) of apamin (5×10^{-7} M).

Kitabgi, Lazdunski & Vincent, 1982*b*). Addition of apamin (5×10^{-7}M) to the bathing solution of rabbit enterocytes abolished the effect of alanine (Fig. 2 and Table 2) and of α-MG (Table 1) on K efflux without affecting the control rates. Quinidine (1 mM), another known blocker of Ca-dependent K permeability (Armando-Hardy, Ellory, Ferreira, Fleminger & Lew, 1975), also abolished the effect of alanine on ^{86}Rb efflux (Table 2).

Ba has been shown recently to block K conductance in several different preparations of epithelial tissue (Nagel, 1979; Welsh, 1983; Kirk & Dawson, 1983). Fig. 3 shows that with isolated rabbit enterocytes 5 mM-Ba abolished any effect of alanine upon K efflux. Contrary to previous findings where Ba reduced basal K conductance (Welsh, 1983) the basal rate of K efflux was not affected by Ba in our experiments.

The successful application of these inhibitors provides useful experimental tools for future investigation, while the results with apamin and quinidine strongly suggest that the increase in K permeability described is mediated by Ca-dependent K channels. The presence of such channels in the small intestine has not been demonstrated previously.

Evidence for Ca-dependent K channels in the intestine and for their involvement in sugar- and amino-acid-induced increases in K permeability

The properties of Ca-dependent K permeability in rabbit enterocytes was further examined using the Ca ionophore A23187. The ionophore was stored as a 10^{-2} M stock solution in dimethyl sulphoxide, dilutions to the required concentration (10^{-5} M) being made in buffer as required. The appropriate control incubations contained an

TABLE 1. Effect of various amino acids on K efflux from rabbit enterocytes

Amino acid (20 mM)	k (/min) Control	+amino acid	n	$k_{a.a.}/k_{control}$
Alanine	0·036±0·016	0·082±0·036	8	2·30
Glutamic acid	0·038±0·007	0·067±0·008	3	1·76
Lysine	0·034±0·005	0·056±0·005	5	1·65
Phenylalanine	0·020−0·024	0·054−0·058	2	2·55
Valine Methionine	0·049	0·099 0·064	1	2·02 1·31
Arginine	0·035±0·006	0·043±0·008	3	1·23

Rate constants (k) in the presence or absence of different amino acids are given. $k_{a.a.}/k_{control}$ is the ratio of the rate constant in the presence of amino acid to that of the control.

Increases by alanine, glutamic acid and lysine, but not that of arginine, are significant by paired t test.

TABLE 2. Effect of apamin or quinidine on the alanine- or α-MG-induced increase in K efflux

	Alanine with apamin		Alanine with quinidine		α-MG with apamin	
Control	0·039±0·006		0·027±0·003		0·035±0·008	
+alanine (or α-MG)	0·066±0·012	$P < 0·02$	0·063±0·009	$P < 0·05$	0·059±0·012	$P < 0·01$
+inhibitor	0·040·±0·008	$P > 0·1$	0·034±0·005	$P > 0·1$	0·033±0·005	$P > 0·1$
+alanine (or α-MG) +inhibitor	0·043±0·009	$P > 0·1$	0·033±0·005	$P > 0·1$	0·029±0·006	$P > 0·1$
n	5		3		4	

The values shown are rate constants (/min) and are means ±S.E. of n experiments.

Concentrations of apamin and quinidine used were 500 nM and 1 mM respectively. Alanine concentration was 20 mM and that of α-MG 5 mM. P values were calculated by paired t test of the significance of the difference with the control value.

equivalent amount of dimethyl sulphoxide. At a concentration of 10^{-5} M, A23187 raised the rate constant of efflux from its basal level of 0·031±0·003/min to a new rate of 0·063±0·004/min ($n = 8$; $P < 0·01$ by paired t test). This is indicative of the presence of Ca-dependent channels. Further evidence is provided by the fact that apamin (5×10^{-7} M) is able to block the ionophore-induced increase in efflux (Fig. 4). Ba used at a concentration of 5 mM also abolished the effect of ionophore (Fig. 5); extracellular (but not intracellular) Ba has been reported to block Ca-activated K channels in isolated pig pancreatic acinar cells (Iwatsuki & Petersen, 1984).

A further indication of the possible role of Ca ions in the observed increase in K

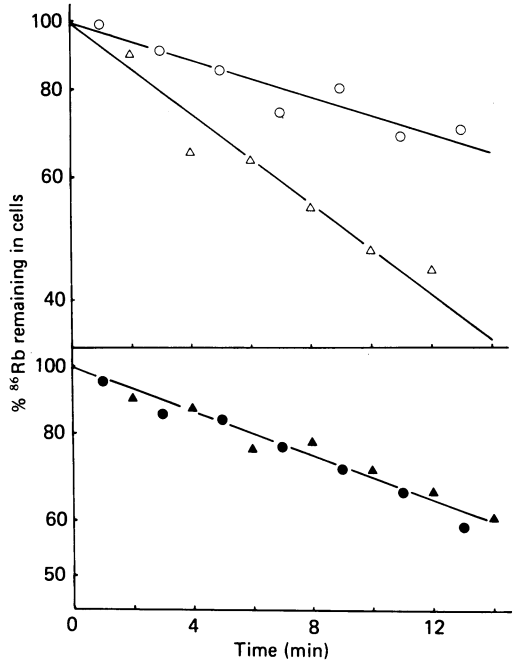

Fig. 3. Effect of Ba on the alanine-induced increase in K efflux from rabbit enterocytes. ^{86}Rb loss was measured in the presence of 20 mM-D-mannitol (○,●) or 20 mM-alanine (△,▲) in the presence (filled symbols) or absence (open symbols) of 5 mM-$BaCl_2$. Other experimental details as in legend to Fig. 1.

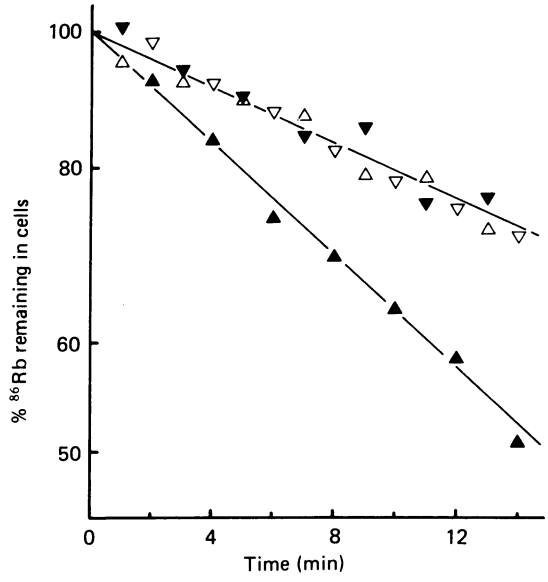

Fig. 4. Effect of apamin on the ionophore A23187-induced increase in K efflux from rabbit enterocytes. ^{86}Rb loss was measured in the presence of 10^{-5} M-ionophore A23187 (▲,▽) or solvent alone (▼,△) and in the presence (▼,△) or absence (▲,▽) of 5×10^{-7} M-apamin.

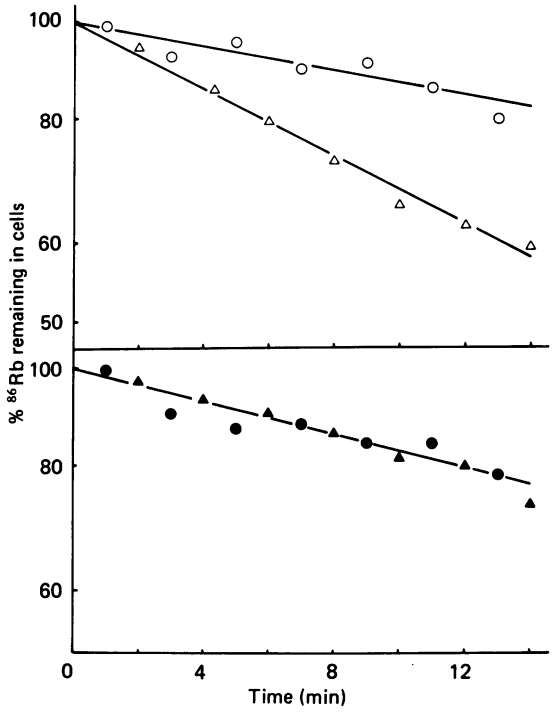

Fig. 5. Effect of Ba on the ionophore A23187-induced K efflux from rabbit enterocytes. ^{86}Rb loss from pre-loaded enterocytes was measured in the presence of 10^{-5} M-A23187 (△,▲) or solvent alone (○,●) in the presence (filled symbols) or absence (open symbols) of 5 mM-$BaCl_2$.

TABLE 3. Effect of trifluoperazine or furosemide on the alanine-dependent increase in K efflux

Inhibitor used	Addition	Control	+inhibitor	Probability
Trifluoperazine	20 mM-mannitol	0·034±0·004	0·032±0·005	$P > 0.1$
Trifluoperazine	20 mM-alanine	0·064±0·005	0·037±0·005	$P < 0.001$
Furosemide	20 mM-mannitol	0·039±0·007	0·038±0·010	$P > 0.1$
Furosemide	20 mM-alanine	0·071±0·008	0·084±0·009	$P > 0.1$

Values shown are rate constants (/min). Significance of difference between control rate constants and those measured in the presence of inhibitors was tested by paired t test. Results are the means ±S.E. of seven experiments for trifluoperazine (5×10^{-5} M) and four experiments for furosemide (10^{-4} M).

efflux was the fact that the calmodulin inhibitor trifluoperazine used at a 5×10^{-5} M concentration inhibited the alanine-induced increased K efflux without affecting the basal rate (Table 3). Verapamil (10^{-5} M), a Ca-channel blocker (Fleckenstein, 1971) also inhibited the effect of alanine, but this was accompanied by a substantial reduction in basal rate of efflux (not shown). Furosemide, a specific inhibitor of the Na–K–Cl co-transport system (Geck, Pietrzyk, Burckhardt, Pfeiffer & Heinz, 1980) had no effect on either the basal rate of K efflux or on the increase provoked by alanine (Table 3).

Effect of sugars and amino acids on intracellular K concentrations

One possible role for the observed increase in K permeability could be helping the enterocyte to maintain an ionic balance while continuing to transport sugars and amino acids from lumen to blood. Using the isolated cells it is possible to assess the effect of amino acid uptake upon the rate of Na–K pumping. Fig. 6 shows the initial rate of ouabain-sensitive K influx into the cells. This rate increased from a control value of $5{\cdot}8 \pm 0{\cdot}7$ nmol/min.mg protein to $10{\cdot}7 \pm 1{\cdot}5$ nmol/min.mg protein in the

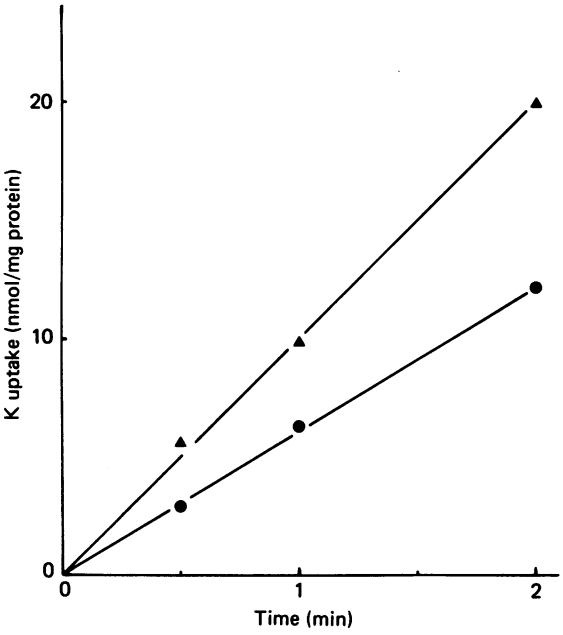

Fig. 6. Ouabain-sensitive K uptake in the presence of 20 mM-D-mannitol (●) or 20 mM-L-alanine (▲).

presence of 20 mM-L-alanine ($n = 8$). The increase in ouabain-sensitive K uptake measured here is of a similar magnitude to that in rat hepatocytes (Van Dyke & Scharschmidt, 1983). Over a 20 min incubation this increase in the rate of K uptake would represent a 50–70 % increase in the K content of the cells.

It has not previously been possible to measure an increase of K uptake in whole rabbit intestine (Nellans & Schultz, 1976) or isolated chicken enterocytes (Sepúlveda, Burton & Brown, 1982) engaged in active transport of sugars or amino acids. Sanders & Misfeldt (1982) have reported that D-glucose increases the rate of ouabain-sensitive K influx in epithelial cells from a pig kidney line (LLC–PK_1). Increases of up to 240 % of the control value have also been reported in cultured rat hepatocytes with amino acids (Van Dyke & Scharschmidt, 1983), where the effect seems to be dependent on the rate of Na entry and on the concentration of Na in the cell.

After a 20 min incubation the K content of the isolated cells was found to equal 164 ± 3 nmol/mg protein (Fig. 7). In the presence of 20 mM-L-alanine there was a fall in the K content of the cells. While 5 mM-Ba alone did not alter the K level in

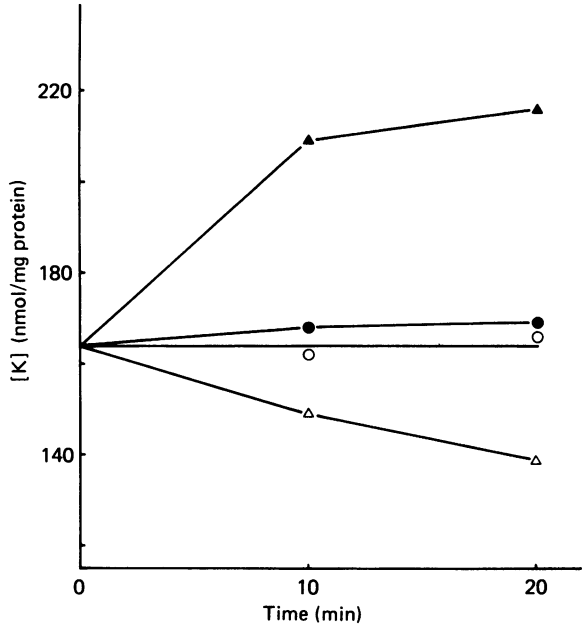

Fig. 7. Intracellular K concentrations in rabbit enterocytes incubated in the presence of 20 mM-mannitol (○), 5 mM-$BaCl_2$ (●), 20 mM-alanine (△) or 20 mM-alanine + 5 mM-$BaCl_2$ (▲).

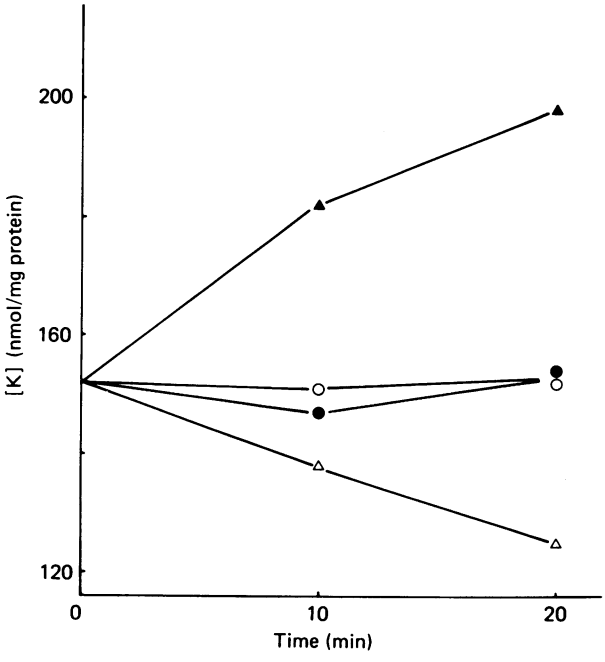

Fig. 8. Intracellular K concentrations of rabbit enterocytes incubated in the presence of 5 mM-mannitol (○), 5 mM-$BaCl_2$ (●), 5 mM-α-MG (△) or 5 mM-α-MG + 5 mM-$BaCl_2$ (▲).

the cells, marked increases were observed when L-alanine and Ba were both present. A similar pattern of events was seen when 5 mM-α-MG rather than alanine was used in the same sort of experiment (Fig. 8). The increases seen with both alanine or α-MG and Ba present are consistent with those that would be expected if the Ba-sensitive pathways were responsible for the dissipation of the extra pump-mediated K influx.

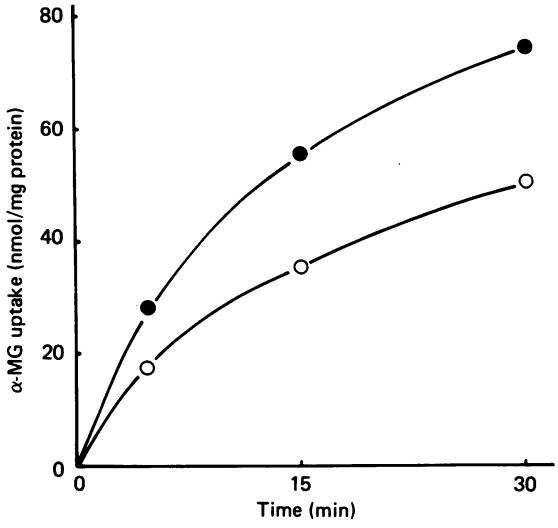

Fig. 9. Phloridzin-sensitive uptake of 2 mM-α-methyl-D-glucoside (α-MG) in the presence (○) or absence (●) of 5 mM-$BaCl_2$.

We have not been able to detect a change in intracellular volume of rabbit enterocytes in the presence of alanine; the apparent volumes were $2{\cdot}26 \pm 0{\cdot}26$ and $2{\cdot}54 \pm 0{\cdot}22$ ($n = 4$) μl/mg cell protein in the absence and presence of 20 mM-alanine respectively. These values were calculated from the steady-state distribution of 3-*O*-methyl-D-glucose attained after a 20 min incubation in the presence of phloridzin. If volume regulation occurred rapidly as a consequence of the observed K movements this would not have been detected by the present technique.

To test whether the change in K permeability might be of importance in the energization of continued active accumulation of sugars the phloridzin-sensitive uptake of 2 mM-α-MG was measured in the absence and presence of 5 mM-Ba (Fig. 9). Ba reduced the accumulation of 2 mM-α-MG to about 60% of the control value after 20 min incubation.

DISCUSSION

The co-transport of sugars and amino acids with Na is known to depolarize the membrane by about 6 mV from a membrane potential of about −36 mV in rabbit small intestine (Rose & Schultz, 1971; Smith, Sepúlveda & Paterson, 1983). Such a decrease could be expected to yield an increase in K efflux of about 15% if the membrane permeability to K remains constant (Goldman, 1943; Hodgkin & Katz, 1949). Since the magnitude of the increase observed here is as much as 16 times

greater, a change in the K permeability of the enterocytes membranes must be postulated to explain this phenomenon. This conclusion is also supported by the results of Grasset *et al.* (1983) who calculated that the steady-state electrochemical potential difference for K across the basolateral membrane of *Necturus* intestinal cells did not change significantly upon addition of alanine.

An increase in permeability was also postulated to underlie amino-acid-induced increases in K efflux from hepatocytes (Kristensen, 1980). In accordance with a premeability change, passive K influx into hepatocytes also increases under these circumstances. Experiments of this nature involve the use of ouabain to eliminate the contribution of the Na pump to K influx and are difficult to interpret in isolated enterocytes where sugar and amino acid transport is instantaneously inhibited in the presence of the glycoside (see fig. 4, Brown & Sepúlveda, 1985; fig. 12, Kimmich, 1975).

A possible mechanism by which the membrane K permeability could be increased is by the operation of Ca-dependent K channels. Such channels have been found in other transporting epithelia (Brown & Simmons, 1982; Petersen & Maruyama, 1984), but not previously in enterocytes. Using the Ca ionophore and known inhibitors of Ca-dependent K channels it has been possible to demonstrate the presence of a similar permeability in cells of the rabbit small intestine. The evidence for the involvement of Ca in the amino-acid- or sugar-induced increase in K permeability, however, is still somewhat circumstantial. A great deal of work needs to be done to confirm the involvement of Ca ions and establish the source of the increased Ca postulated to exist within the cell. To actually measure an increase in intracelluar Ca activity in the presence of sugars and amino acids would be an important finding. The fluorescent indicator Quin 2 allows Ca activity to be measured without recourse to a disruptive manipulation of the cells (Tsien, Pozzan & Rink, 1982), but unfortunately preparations of isolated rabbit enterocytes appear to contain a great deal of extracellular esterase activity and most of the lipophilic acetoxymethyl Quin 2 ester is hydrolysed before it is able to enter the cell (F. V. Sepúlveda, unpublished results). Increases in Ca ion activity have, however, been shown with Quin 2 in toad bladder epithelial cells during periods of increased Na entry at the apical membrane (Crutch & Taylor, 1983). Increased Na entry might provide substrate for a Na–Ca exchange mechanism at the basolateral membrane leading to this increase (Taylor & Windhager, 1979) and a similar chain of events could be triggered, in the enterocyte, when Na influx is increased during coupled transport of sugar or amino acids. Basolateral membranes isolated from rat enterocytes have been reported to possess a Na–Ca exchange system (Ghijsen, De Jong & Van Os, 1983) and such a mechanism might be involved in the generation of a signal for increased K efflux.

Changes in cell volume can also initiate events leading to K and Cl efflux from many cell types (Kregenow, 1977). Bakker-Grunwald (1983) and Kristensen & Folke (1984) have attributed the increase in K efflux in hepatocytes actively transporting amino acids (Kristensen, 1980) to a volume-regulatory event in response to amino acid accumulation. Kristensen & Folke (1984) also demonstrated that, in agreement with present results, this alanine-dependent increase in K efflux in hepatocytes was abolished by quinidine and not affected by furosemide. Ca-activated K channels are thought to be involved in volume regulation in lymphocytes (Grinstein, Dupre &

Rothstein, 1982) and in Ehrlich ascites tumour cells (Hoffman, Simonsen & Lambert, 1984). Although activation of K permeability could result in volume regulation, the intracellular signalling involved might be other than the pure change in volume. The results in Figs. 8 and 9 of the present work suggest that the increase in K permeability could be crucial to the regulation of cell volume by preventing a build-up of cellular K but it would be difficult to establish whether this is due to an initial change in cell volume.

As the response to changes in cell volume would presumably be electrically 'silent', even if it occurred through functionally separate K and Cl channels (Sarkadi, Mack & Rothstein, 1984; Hoffmann *et al.* 1984), it would be appropriate in the present case if the increase in K efflux was more directly linked to Na transport associated with sugar and animo acid uptake. Certainly the results in Table 1, where it is shown that amino acids whose transport is highly Na-dependent cause the greatest increases in K efflux, support this hypothesis.

The increase in K efflux also appears to be closely linked to the rate of Na and K pumping by the cells, as the Ba-sensitive channels appear to dissipate the effects of extra K influx at times of increased pumping (Fig. 8). Similar conclusions have been reached by Schultz (1981), Grasset *et al.* (1983) and Smith & Frizzell (1984) who believe that the K conductance of the basolateral membrane, measured electrophysiologically, increases in parallel with pump activity.

The increased K permeability was proposed to be an innate property of the Na–K pump in the previously cited papers. Anner (1981) has shown in reconstitution experiments that the incorporation of Na–K ATPase in liposomes increases their passive permeability to K. We do not favour this hypothesis for the phenomenon observed here since the effect of amino acid can still be observed, although to a reduced extent, in the presence of ouabain (P. D. Brown & F. V. Sepúlveda, unpublished results) and because the Na pump and the Ca-activated K channel have been shown to be separate in other cells (Karlish, Ellory & Lew, 1981).

Apart from dissipating extra pump-mediated K influx, the increase in K permeability may also be responsible for the energization of sugar and amino acid transport in the intestine (Schultz, 1981). Ba inhibits α-MG accumulation by 40% (Fig. 9) suggesting that the Ba-sensitive channels have a role in energizing transport in isolated rabbit enterocytes. If the Ba-sensitive channels were electrogenic, it could explain both the effect of Ba on α-MG accumulation seen here and the repolarization effect observed by Albus (1981) and Gunter-Smith *et al.* (1982). In fact a very recent paper by Lau, Hudson & Schultz (1984) shows that Ba inhibits the change in basolateral membrane resistance and repolarization observed in the presence of sugars and amino acids in *Necturus* small intestine. This suggests that the phenomenon described in the present paper might also be related to the electrical transients described previously.

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